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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/160,076	09/24/1998	DAVID W. SCOTT	308072000110	5918

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/160,076	SCOTT ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-74 and 76-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-74 and 76-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 75 has been cancelled. Claims 69-74 and 76-81 remain pending and under consideration in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant's arguments filed 2-26-04 have been fully considered but they are not persuasive.

Support for "allergens" in claim 81 can be found on pg 10, lines 24-25.

Specification

The first line of the specification has been updated.

The blanks on pg 16 have been filled in.

The title has been amended.

Claim Rejections - 35 USC § 112

Claim 70, 72, 74, 80 and 81 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Claim 70 remains indefinite because claim 69 does not require that the nucleic acid sequence was introduced into the cell. Therefore, the phrase "wherein said nucleic acid was introduced into the cell" in claim 70 does not make sense. The phrase "wherein said nucleic acid sequence is a viral vector" would overcome this rejection. Applicants have traversed this rejection but have not argued this rejection.

The rejection of claim 72 regarding the structure of the limitation being unclear has been withdrawn in view of the amendment to the claim.

The rejection regarding the phrase "the first framework region of said N-terminal variable region" (claim 74) lacking antecedent basis in parent claims 69 or 70 has been withdrawn in view of the amendment to claim 74.

The rejection regarding "first framework region" has been withdrawn because applicants state it was known in the art that there were four framework regions, and the amino-terminal framework region is the first framework region (¶ bridging pg 7-8 of response).

The term "autoimmune antigen" (claim 80) remains indefinite for reasons of record regarding autoantigen. The prosecution of the rejection has been reiterated by applicants but does not add any new arguments. The definitions of "autoantigen" do not aid in defining the metes and bounds of the term because they are conditional upon the host in which they are found. Applicants' definition is the basis of the confusion. To further clarify the examiner's position, if one of skill isolated MART-1 from a patient with melanoma who did not have an autoimmune response against MART-1, it would be unclear whether that MART-1 would be an autoimmune antigen as claimed because it did not induce an autoimmune response. If one of skill isolated MART-1 DNA from a melanoma patient that did not have an immune response against MART-1 and used it to make the pharmaceutical composition claimed, it is unclear if they would be infringing on the claimed invention because that particular MART-1 did not induce an autoimmune response. It is unclear whether the term merely refers to any protein having a structure

that is the same as a protein known to induce an immune response in some patients or if the term is limited to only proteins isolated from patient that induce an immune response against the protein.

The rejection of claim 81 regarding the term "allergan" has been withdrawn in view of the amendment.

Claim 81 is newly rejected because "allergen" does not further limit the "antigen" of claim 69. Any "antigen" may be an "allergen" (see definition of "allergen" attached).

Claim Rejections - 35 USC § 102

Claims 69 and 79-81 remain rejected under 35 U.S.C. 102(b) as being anticipated by McDonnell et al. (Cell, 1989, Vol. 57, pg 79-88) for reasons of record.

McDonnell taught a transgenic mouse whose genome comprised a transgene comprising bcl-2-Ig fusion protein. Splenocytes and thymocytes were isolated from the mice in saline and media. The splenocytes and thymocytes are non-tumor lymphoid cells and are equivalent to the composition claimed because they have the structure claimed. The bcl-2-Ig fusion protein is equivalent to the fusion protein required in the claim because it has a heavy chain immunoglobulin and bcl-2. The bcl-2 protein inherently has at least one epitope as claimed. The cells of McDonnell inherently "induce tolerance to an antigen" because it has the same structure as the cell claimed. The phrase "suitable for introduction into an individual" does not bear patentable weight because it is an intended use and may not occur. The intended use does not bear patentable weight because it does not alter the structure of the composition. The

composition of McDonnell inherently meets the functional limitation of "wherein upon introduction to the individual said composition induces tolerance to the antigen in the individual" because it has the structure claimed. The splenocytes and thymocytes inherently comprise "hematopoietic cells" (claim 79) because they comprise pluripotent cells capable of differentiation. Claim 80 is included because the metes and bounds of the term "autoimmune antigen" cannot be determined (see 112/2nd). Bcl-2 is an allergen as newly amended (claim 81) because it would be recognized as foreign in non-mammalian species and would induce an immune response in the non-mammalian species that inhaled the protein. The definition of "allergen" states "[n]o comprehensive list of allergens is possible, because sensitivities vary from one person to another and it is possible to be allergic to literally anything" (see attached definition).

Applicants argue the examiner has not provided evidence that the minigene of McDonnell encodes a fusion protein as claimed (pg 12, 1st full ¶). applicants' argument is not persuasive. Pg 80, Fig. 1, of McDonnell clearly shows the minigene encodes a fusion protein having a heavy chain Ig and bcl-2. it is unclear why applicants believe this minigene does not encode an immunoglobulin fusion protein. See pg 81, Fig. 2, which describes a Bcl-2-Ig transgene RNA of 401 bp that was transcribed in the mice.

Applicants argue McDonnell does not teach that a bcl-2-Ig fusion protein is expressed (pg 12, 1st full ¶). First, applicants' argument is moot because the claims do not require expression. Second, applicants' argument is not persuasive because pg 80, col. 2, specifically refers to bcl-2-Ig minigene expression and pg 81, Fig. 2 confirms expression by detecting a 401 bp RNA transgene fragment comprising Bcl-2 and Ig.

See also lines 1-2 of pg 81 which states [t]he M-43 transgenic line also displayed expression of bcl-2-Ig NL in the lung...."

Applicants argue McDonnell did not teach genomic rearrangement within the heavy chain so that Ig sequences are properly translated (pg 13, lines 1-10). First, applicants' argument is moot because the claims do not require genomic rearrangement or proper translation. Second, Fig. 2 on pg 81 shows the RNA was processed as desired into a bcl-2–Ig 401 bp fragment. There is no reason to believe this fragment of the desired and expected size after splicing would fail to be properly translated. Especially in view of the fact that the mice had a phenotype that was different than normal or those expressing just bcl-2 or just immunoglobulin.

Applicants argue the examiner has not demonstrated that the composition of McDonnell inherently "induces tolerance to the antigen" in an individual (pg 13, item 2). Applicants' argument is not persuasive because the specification states any expression cassette having a sequence encoding a fusion immunoglobulin having a "tolerogenic epitope" at the N-terminus variable region (pg 8, lines 5-10). The description of "tolerogenic epitopes" on pg 11, line 4, through pg 12, line 11, does not exclude bcl-2. The description of "tolerogenic epitopes" essentially encompasses any protein. This is clear from the specification, which teaches bacterial λ-CI repressor protein was a "tolerogenic epitope." While λ-CI repressor protein was a protein used merely for lab studies, one of skill would not desire to "tolerize" an individual to λ-CI repressor protein.

Applicants argue the cells are not suitable "for introduction to an individual" because they may cause tumors (pg 14, item 3). Applicants' argument is not

persuasive. Non-tumor lymphoid cells having genes that cause tumors can be introduced into a lab mouse. Cells that cause tumors are well "suitable for introduction to" a lab mouse. In fact, McDonnell created a mouse in which every cell expresses a gene that causes tumor. Therefore, it was well known in the art at the time of filing that cells expressing a gene that caused tumors could be introduced into lab mice. Anything, including cells encoding a tumor-causing protein, can be introduced into a lab mouse.

Applicants argue the cells were not in a pharmaceutical composition (pg 15, item 4). Applicants' argument is not persuasive. Splenocytes and thymocytes were suspended in saline and media, which are pharmaceutically acceptable carriers. Applicants argue that HBSS, DMEM or PBS as disclosed on pg 86, right column, are not pharmaceutically acceptable excipients. Applicants' argument is not persuasive because HBSS, DMEM and PBS have a physiological pH and can be injected into the mice. In addition, DMEM supports cell growth by providing nutrients found *in vivo*. Injection of cells with HBSS and DMEM into mice would not cause the cells to die or the mice to die. Applicants have provided no reasoning why a "pharmaceutically acceptable excipient" would exclude HBSS, DMEM or PBS. The claims do not exclude adding other ingredients such as penicillin-streptomycin, calf serum and antibodies. It is unclear why applicants believe the addition of other ingredients to HBSS, DMEM or PBS makes the solution no longer pharmaceutically acceptable.

Applicants argue the splenocytes of McDonnell do not comprise hematopoietic cells (pg 17). Applicants' argument is not persuasive. Splenocytes comprise T-cell

progenitors, for example, that differentiate into mature helper T cells and cytotoxic T cells. Furthermore, Nishijima (1997, Blood, Vol. 90, pg 1031-1038) taught normal and transgenic mice had hematopoietic cells in their spleen (pg 1034, col. 2, 1st full ¶).

Double Patenting

The objection to claim 75 under 37 CFR 1.75 as being a substantial duplicate of claim 70 has been withdrawn because claim 75 has been cancelled.

Claim 81 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 69. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The term "allergen" in claim 81 does not further limit the antigen in claim 69 because any "antigen" may be an "allergen" (see definition of "allergen" attached). Therefore, the scope of claims 69 and 81 are the same.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claim is allowed.

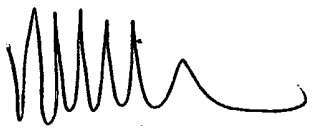
Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson



MICHAEL WILSON
PRIMARY EXAMINER